reproductive cycle (Wilting and Christ, (1996) Naturwissenschaften **83**:153-164; Goodger and Rogers, (1995) Microcirculation **2**:329-343; Augustin et al., (1995) Am. J. Pathol. **147(2)**:339-351). Some of the important steps in the process of angiogenesis are: 1) growth factor (i.e. vascular endothelial growth factor, VEGF) signaling; 2) matrix metalloproteinases (MMP) and VEGF receptor interaction; 3) endothelial cell migration to site of growth factor signaling; and 4) endothelial cell tubule formation. Pathological angiogenesis play a central role in a number of human diseases including tumor growth and metastatic cancer, diabetic retinopathy, rheumatoid arthritis, and other inflammatory diseases such as psoriasis (Folkman, (1995) Nature Med. **1(1)**:27-31; Polverini, (1995) Crit. Rev. Oral Biol. Med. **6(3)**:230-247; Walsh, (1999) Rheumatology **38(2)**:103-112; Healy et al., (1998) Hum. Reprod. Update **4(5)**:736-740). In these cases, progression of disease is driven by persistent unregulated angiogenesis. For example, in rheumatoid arthritis, new capillary blood vessels invade the joints and destroy the cartilage. In diabetic retinopathy, capillaries in the retina invade the vitreous, bleed and cause blindness. Significantly, tumor growth and metastisis are angiogenesis dependent. Most primary solid tumors go through a prolonged avascular state during which growth is limited to approximately 1-2 mm in diameter. Up to this size, tumor cells can obtain the necessary oxygen and nutrient supply by passive diffusion. These microscopic tumor masses can eventually switch on angiogenesis and recruit surrounding blood vessels to begin sprouting capillaries that vascularize the tumor mass, providing the potential for continuing expansion of the tumor and metastasis of malignant cells to distant locations. Although significant progress has been made in understanding the biological events that occur during pathological angiogenesis, there are presently no effective pharmaceutical compounds that are useful for controlling angiogensis *in vivo*. Thus, effective therapies capable of controlling angiogenesis have the potential to alleviate a significant number of human diseases.--

Please replace paragraph 0072 at page 18, with the following rewritten paragraph:

--Example 3

Endothelial Cell Assays (CPAE")

The assays were carried out according to the procedures of Connolly, et al. (1986) Anal. Biochem. **152**:136-140 with modifications (Liang and Wong (1999) ANGIOGENESIS: FROM THE MOLECULAR TO INTEGRATIVE PHARMACOLOGY edited by Maradoudakis, Kluwer Academic/Plenum. Publishers, New York). Calf Pulmonary Arterial Endothelial (CPAE) cells are plated at 10,000 cells per well in 24 well culture plates. After growth incubation at 37°C, 5% CO_2 for about 60 hours, a dosage of the sample is added (about 50µl to about 100µl) to each sample well and re-incubated for 30 minutes. After incubation, cells are assayed visually under an inverted microscope to detect the presence of cells and through the use of the ECC assay. Both methods are used to detect the presence or absence of endothelial cells in each well. Control cells containing no sample were used and grew normally. –

Please replace paragraph 0074 at page 19, with the following rewritten paragraph:

--**Example 5**

MMP Assay

P.C. Brooks, et. al. (1996) in "Localization of matrix metalloproteinase MMP-2 to the surface of invasive cells by interaction with integrin αvβ3," (1996) Cell **85**:683-93 describes an *in vitro* assay on matrix metalloproteinase and αv/β3 integrin interaction. The effects of the experimental sample on the MMP-2/αvβ3 integrin complex determines if the sample's mechanism of action involves any disruption of this segment of the angiogenic pathway. This involves testing if the experimental sample can inhibit the interaction of MMP-2 with the αvβ3 integrin. Initially, this is done via an ELISA using antibodies for MMP-2 and testing the binding of these antibodies to the sample. Further studies are pursued if a positive result occurs. TIMP-2 (Tissue Inhibitor of Matrix Metalloprotease-2), a known natural inhibitor of MMP-2, is used as the control.--

REMARKS

Paragraphs 0004, 0072 and 0074 of the specification have been amended to correct typographical errors.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

In the unlikely event that the transmittal letter is separated from this document and/or the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-1189**, referencing attorney billing